Remarks

This amendment is in response to the Office Action mailed September 16, 2005. Claims 1-100 are pending. By this amendment, claims 1, 8, 15, 37, 44, 51, 56, 67, 78, and 90 are amended, and new claims 101 through 104 are added. In addition, the specification is amended to comply with the Examiner's objection.

The items raised in the Office Action are addressed in the remarks below.

I. Oath / Declaration

The Examiner rejected claims 1-100 as being based upon a defective reissue oath under 35 U.S.C. § 251. The Examiner's grounds for this rejection are noted, and the defect has been corrected in the "First Amended Joint Declaration" of the inventors submitted with this amendment. Specifically, paragraph 4 has been amended to state that the inventors "believe the '098 Patent to be partly inoperative or invalid ...."

II. Information Disclosure Statement

An IDS listing all references in application 09/519,950 that appear on the face of US Patent No. 6,346,098 is submitted herewith, in compliance with the Examiner's request.

III. Specification

The specification has been corrected by this amendment in compliance with the Examiner's objection. Specifically, the references to "Fig. 1" have been changed to "Fig. 2" in the paragraph extending from column 3, line 66 to column 4, line 35.

IV. Claim Rejections – 35 U.S.C. § 102

A. Makower

Claims 1-10, 12-17, 20, 24, 28, 30-35, 36-46, 48-54, 56-58, 61-70, 72-82, 84-93, and 95-100 were rejected under 35 U.S.C. § 102(e) as being anticipated by Makower et al. (US 2002/0179098). Applicants respectfully request reconsideration of this rejection.

As the Examiner states in the office action, the Makower publication describes methods of Transmyocardial Direct Coronary Revascularization (TMDCR) in which a passageway-forming catheter is advanced through the coronary vein or artery and is used to create interstitial passageways. The Examiner also states that the described methods include "locally administering an active agent such as blood, oxygen, autologous or xenograft tissue ... in which the agent is retroinfused into a vascular vessel such as a vein under conditions sufficient to disrupt the vein such that the agent enters interstitial space ...." In the Makower publication, however, it is the passageway-forming catheter that is used to "disrupt" the vein. The "active agents" listed by the Examiner play no part in the disruption process, they are only introduced after the disruption (more precisely, tissue penetration) has taken place.

On the other hand, by the present amendment, each of the independent claims of the present reissue application recite that it is "the agent or a fluid delivery vehicle thereof" or "a fluid" that produces the disruption, mechanical stress, or distention of the vessel. This is neither taught, disclosed, nor suggested by the Makower publication. Accordingly, because the Makower publication fails to disclose every element of the claims at issue, those claims are patentable over and above the Makower publication. Applicants respectfully request withdrawal of the rejection of those claims under section 102(e).

B. Wolff

Claims 1-3, 7-11, 13-19, 21-23, 29, 30-34, 36-39, 43-47, 49-59, 61-70, 72-82, 84-93, and 95-100 were rejected under 35 U.S.C. § 102(e) as being anticipated by Wolff et al. (USP 6,867,196). Applicants respectfully request reconsideration of this rejection.

As the Examiner states in the office action, the Wolff patent teaches methods of delivering nucleic acids to cardiac tissue using a channel leading to cardiac tissue from a vessel. The Wolff patent, however, teaches methods that do not include disruption of the vessels. Wolff, instead, teaches methods that are expressly intended to avoid such damage:

> The target bed size in the heart will vary from case to case. In order to correlate variations in the injection parameters with expression, determination of the bed size is important. This can be done by injection of iodinated contrast detected by fluoroscopy. By performing this procedure prior to each plasmid DNA injection, gene transfer efficiency is expressed per total target bed size. It also allows for prediction of the required injection volume and speed. In one preferred embodiment (i.e., plasmid DNA extravasation and

> myocyte transfection), a threshold volume in a set time is exceeded and then maintained for a short time. This will form a square wave form on a plot of intravenous volume versus time. To reach the threshold, a larger injection volume or higher injection speed is required for a larger target bed. Therefore, an automatic injection system can be used to inject the plasmid DNA solution until this pressure threshold is reached and then maintain at or above this threshold for a given time. By creating a feedback between the intravenous pressure at the site of injection and the injection pump, a system can be created that automatically senses the target bed size and inject the proper amount of transfection solution. By limiting the injection volume per time unit, minimal tissue damage is incurred. All of the pigs injected recovered well from the procedure, and little damage was observed. ***Tissue sections from the injection site and stained with hematoxylin-eosin did not show any major histological abnormalities.***

(Wolff patent, col. 6, line 52 to col. 7, line 11). The highlighted section above demonstrates that the methods taught by Wolff are intended not to disrupt the vessel wall.

In addition, the Wolff patent does not teach the use of energy in the agent administrative method.

On the other hand, each of the independent claims of the present application recites either that the method includes the step of producing a disruption in the vessel (claims 1, 8, 15, 37, 44, and 51) or that the method includes the administration of energy to the vessel (claims 56, 67, 78, and 90). Neither of these method steps is disclosed, taught, nor suggested by the Wolff et al. patent. Accordingly, because the Wolff et al. patent fails to disclose every element of the claims at issue, those claims are patentable over and above

the Wolff et al. patent. Applicants respectfully request withdrawal of the rejection of those claims under section 102(e).

IV. Claim Rejections – 35 U.S.C. § 103

The Examiner rejected claims 1 and 25-27 under 35 U.S.C. § 103(a) as being unpatentable for obviousness over the Wolff et al. patent. The Examiner states that:

> It would have been obvious to someone of skill in the art to utilize pressure of at least 50 mm Hg, 60 mm Hg and 1000 mm Hg in the method of Wolff et al given that the identification of these pressures would be required to optimize the hydrostatic pressure to permeabilize or disrupt the vessels for deliverance of the agents.

To begin with, Applicants respectfully disagree with the Examiner's contention to the extent that any of the foregoing pressures would produce disruption of a vessel. As noted above, Wolff et al. explicitly teach not to damage the vessel or other tissue, as would occur if the vessels are disrupted.

In addition, as noted above, the Wolff et al. patent fails to disclose, teach, or suggest methods that include disruption of the vessel, or the administration of energy to the vessel. Because these limitations are not met by the art relied upon by the Examiner, there has been no prima facie showing of obviousness. Accordingly, Applicants respectfully request withdrawal of the rejection of these claims under section 103(a).

SPECIFICATION SUPPORT AND STATUS OF CLAIMS

Specification support for all of the amendments and new claims is listed in the "Statement of Status / Support for Changes to Claims (Amendment Dated March 16, 2006)" submitted herewith. No new matter is added by this amendment.

CONCLUSION

In view of the foregoing, it is submitted that the claims presented in this reissue application define patentable subject matter to which Applicant is entitled. Accordingly, consideration and allowance of the reissue application is requested.

The Commissioner is authorized to charge any fee which may be required in connection with this Amendment to deposit account No. 15-0665.

Respectfully submitted,

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